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10/595,709	05/05/2006	Felicia Grases Freixedas	OFICINA-256657	5118

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Cozen O'Connor
277 PARK AVENUE
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EXAMINER

CHANNAVAJJALA, LAKSHMI SARADA

ART UNIT	PAPER NUMBER
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1611

NOTIFICATION DATE	DELIVERY MODE
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12/30/2011

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/595,709	Applicant(s) GRASES FREIXEDAS, FELICIA	
	Examiner LAKSHMI CHANNAVAJJALA	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.
- 4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) ☒ Claim(s) 8-19 is/are pending in the application.
- 5a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 6) ☐ Claim(s) ____ is/are allowed.
- 7) ☒ Claim(s) 8-19 is/are rejected.
- 8) ☐ Claim(s) ____ is/are objected to.
- 9) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 10) ☐ The specification is objected to by the Examiner.
- 11) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Receipt of response dated 10/10/2011 is acknowledged.

Claims 8-19 are pending in the instant application.

The following rejection of record has been maintained:

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claims 8-19 are rejected under 35 U.S.C. 102(b) as being anticipated by US 5,268,176 to Znaden et al as evidenced by James et al. (Radiographic, 1999, pages 1093-1099).
3. Znaden patents teach topical preparations comprising phytic acid in the amounts of 5-50% or at least 3% (176 patent, examples, claims 3-4 and col. 3, l 27-41). Znaden reference ('176) teaches the penetration of the compound through the skin layers (col.3, l 1-11). While Znaden 176 patent teaches the composition for topical treatment of spider veins (telangiectasia or spider veins- see abstract and col. 1-2), and not the claimed method of treating tissue calcification, James (Radiographics) teaches the occurrence of soft tissue calcifications in patients with varicose veins (see page 1093 col. 1-2, History and Findings). This is further described on page 1095, col. 1. Instant claims are not limited to any specific patient population and hence may include patient population with varicose veins. "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the

Art Unit: 1611

claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Applicants previously argued the rejection of instant method claims over the above Znaiden patent (**page 6 of the remarks of 2/5/08**). However, in the present rejection, the examiner provided evidence that varicose veins and soft tissue calcification can coexist in patients and instant claims do not exclude such population. Applicants previously argued that the above reference teaches phytate for being sequestered in the skin layers as a depot, whereas "[s]urprisingly, the inventors of this invention have found that phytate, with a high negative charge, can be absorbed by the skin when it is administered topically, passing through into the bloodstream and acting on the damaged zone (in which a heterogeneous nucleant would have been generated)." Applicants submit that Znaiden does not teach a method of treatment or prevention wherein the phytate is absorbed through the skin into the bloodstream, as disclosed in new Claims 8- 19, and does not disclose every element of the claims, Applicants respectfully request the Examiner reconsider and withdraw the rejection under 35 U.S.C. § 102(b).

Instant claims recite the composition only with myo-inositol hexaphosphate or its salts and do not recite any formulation. Therefore, if applicants if the same compound of the prior art (by virtue of its chemical properties) does not penetrate through skin layers for absorption, then for the same reason instant compound also should fail to penetrate. However, Znaiden while teaching that the compound is sequestered in the skin layers,

Art Unit: 1611

Znaiden also teaches a "formulation" containing the compound, which can enable its penetration and absorption. In this regard, if applicants' "unexpected absorption" (which is otherwise not possible with the compound based on Znaiden's teaching) is due to the presence of other penetration and/or absorption enhancers in the claimed composition, then the examiner notes that instant claims are silent regarding such penetration and absorption aids and absent such the composition of Znaiden reads on the instant composition. Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

If applicants argue that the claimed method is not inherent to Znaiden et al ('176 patent), then the following rejection based on obviousness is applied:

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Art Unit: 1611

5. Claims 8-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over any one of US 5,552,148 or US 5,268,176 both to Znaiden et al, in view of Horrobin et al. (US patent 5,516,801), and Kamiya et al. (US Patent Application Pub. No. 2003/0119910), and further in view of James et al. (Radiographics, 1999, pages 1093-1099).

6. Znaiden patents teach topical preparations comprising phytic acid in the amounts of 5-50% or at least 3% (176 patent, examples, claims 3-4 and col. 3, l 27-41) or '148 patent teaches 0.001% to 40% or preferably 0.5%-10% (col. 2, l 38-52 and examples). While Znaiden 176 patent teaches the composition for topical treatment of spider veins (telangiectasia or spider veins- see abstract and col. 1-2), and '148 as a cosmetic additive, neither teach the claimed method of treating tissue calcification. However, 148 suggest the compound for various therapeutic methods (see col. 1) such as spider veins, acne etc.

7. While instant claims require topical administration of phytic acid, the claims do not recite the actual amount and further only states "pathological calcification treating effective amounts" of phytic acid. The examples in the instant specification recite 2.9%; 0.7% and 2.5% (pages 7-9) for topical application.

8. Kamiya et al. teach methods of treating or preventing aging-associated diseases caused by a decrease in the expression of Klotho protein in animals or humans, including aging, ectopic calcification, skin involution, arteriosclerosis, hyperlipidemia, hypertension, cerebral apoplexy, diabetes, senile dementia of Alzheimer type (para 0022-0023). In particular, Kamiya et al. teach compositions comprising phosphorus

Art Unit: 1611

containing compounds, such as phytic acid, for treating said diseases in animals or humans (abstract; para. 0081). Also, Kamiya et al. disclose that it is desirable to administer said compositions by any desirable route that is most effective for the treatment, including non-oral routes (para. 0044). Kamiya teaches an amount of 0.5% to 5% or more per unit dry weight of food or feed drink.

9. James (Radiographics) teaches the occurrence of soft tissue calcifications in patients with varicose veins (see page 1093 col. 1-2, History and Findings). This is further described on page 1095, col. 1.

10. Horrobin et al. is added as an evidentiary reference to show that ectopic calcifications involve various soft tissues, including blood vessels, kidney, skin, and brain (col. 2, lines 14-32).

11. Thus, one of an ordinary skill in the art would have been able to employ the topical compositions comprising phytic acid of Znaiden references for treating varicose veins and still expect to achieve a therapeutically effective treatment for soft tissue calcification because James et al teach that the patients with varicose veins also exhibit soft tissue thickening and calcification and further because Kamiya teaches treating or preventing aging-associated diseases caused by a decrease in the expression of Klotho protein in animals or humans, including aging, ectopic calcification, by administering phytic acid. This is further true because instant claims do not exclude the patient populations with varicose veins (Znaiden) or other age related problems other than ectopic calcification (Kamiya).

Art Unit: 1611

12. Instant claims recite the composition only with myo-inositol hexaphosphate or its salts and do not recite any formulation. Therefore, if applicants if the same compound of the prior art (by virtue of its chemical properties) does not penetrate through skin layers for absorption, then for the same reason instant compound also should fail to penetrate. However, Znaiden while teaching that the compound is sequestered in the skin layers, Znaiden also teaches a "formulation" containing the compound, which can enable its penetration and absorption. In this regard, if applicants' "unexpected absorption" (which is otherwise not possible with the compound based on Znaidens' teaching) is due to the presence of other penetration and/or absorption enhancers in the claimed composition, then the examiner notes that instant claims are silent regarding such penetration and absorption aids and absent such the composition of Znaiden reads on the instant composition. Products of identical chemical composition cannot have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

13. Further, one would reasonably expect that the topical administration/application to the skin of a composition comprising the instantly claimed myo-inositol hexaphosphate (phytic acid) as taught by Znaiden or Kamiya et al. would be absorbed

Art Unit: 1611

by the skin and then travel via the bloodstream to the target site where the calcification is generated, including the sub epithelial tissue, renal tissue, pulmonary tissue, cerebral tissue, and the wall of a blood vessel because Kamiya et al. and Znaiden references teach therapeutically effective compositions containing phytic acid. Besides, Kamiya et al. teach compositions for treating aging-associated conditions (e.g. skin wrinkles), which overlaps with the instant claimed population (i.e. ectopic calcification) as evidenced by the teaching of Kamiya et al. and Horrobin et al.

14. With respect to the preamble of claim 14, it is noted that Kamiya et al. teach methods for preventing aging-associated diseases, including ectopic calcification, comprising administering compositions comprising phytic acid (para. 0081). A skilled artisan would have expected to prevent the development of calcification from the teachings of Znaiden, for the reasons mentioned above.

15. With respect to the limitations recited in dependent claims 9-13 and 15-19, it is noted that Kamiya et al. teach aging-associated diseases including ectopic calcification, which overlaps with the instant claimed population (pathological calcification in a soft tissue). Since ectopic calcification involves soft tissues, including skin, brain, kidney, and blood vessels, one would reasonably expect that the method of treatment comprising topically administering the same instantly claimed compound as taught by the prior art would also be effective in treating/ preventing pathological calcification involving sub epithelial tissue, renal tissue, pulmonary tissue, cerebral tissue, and the wall of a blood vessel as evidenced by the teaching of Horrobin et al. (col. 2, lines 14-32).

Response to Arguments

Applicant's arguments filed 10/10/11 have been fully considered but they are not persuasive.

Applicants argue that varicose veins and spider veins are different and also have different treatments as evidenced by the information provided on the website for the National Center for Biotechnology Information and the website <http://www.spiderveinsonlegs.org>. Applicants argue that James reference teaches nothing more than the medical fate of a single 15-year- old patient afflicted with Klippel-Trenaunay syndrome, as reflected in the reference's title "Pediatric Case of the Day." In relevant part, this patient was afflicted with varicose veins and calcified phleboliths, among other disorders. It is argued that based on the singular example in James, one cannot reasonably conclude that a subject having varicose veins is necessarily afflicted with soft tissue calcification. Nothing in James suggests otherwise.

Applicants' arguments are not persuasive because first, instant claims are not limited to any particular patient population nor the claims are limited to patients who do not possess varicose veins. Applicants have not provided evidence that varicose veins and tissue calcification are mutually exclusive. According to the instant claims, it is possible that soft tissue calcification can occur in any subject including people with varicose veins and/or spider veins. Second, while applicants provided evidence to describe both varicose and spider veins that have different manifestations, there is no evidence in the cited websites that a treatment for one condition does not suffice for the other. Additionally, examiner herewith cites the information provided on

Art Unit: 1611

<http://www.perfectleg.com> to show that the most important component to any successful varicose vein surgery needs to be the elimination of the leaking valves that led to the varicose veins and spider veins in the first place. Without complete elimination of ALL these tiny "waterfalls" the veins and spiders will recur. Whether due to pregnancy, weight gain or heredity, the valves become weakened and leak, leading to varicose veins and spider veins. It is stated that the technique employed therein (Harvester technique) reduces swelling in legs with no spider or varicose veins. The above web site states:

"Our technique to create near perfect legs in over 99% of the patients is based on 25 years of experience in permanent treatment of varicose veins. This patented technique (Harvester technique) takes about 15 minutes and is done entirely in an office set up without any disability or any major anesthesia. None of the other techniques have the safety and efficacy of this approach. The end result is a thinner leg (lack of swelling) with no varicose veins or spiders."

Thus, both spider and varicose veins have a common symptom and starts with dilated veins. Accordingly, one may provide a common method of treatment and/or prevention for both conditions or treat them by different methods. As mentioned above, instant claims do not limit the patient population in which soft tissue calcifications occur. Thus, the examiner maintains that the claimed method is inherent in the teaching of Znaiden i.e., topical application of phytic acid.

Applicants argue that according to Znaiden, phytic acid is a highly polar and accordingly, instead of dissipating to enter the body systemically, it remains in the intercellular space of the cell membrane. Therefore, applicants argue that one of an ordinary skill in the art would have expected the claimed methods to fail due to phytate sequestration in the intracellular space and also for the fact that it is hard for the salt

Art Unit: 1611

form of an acid to penetrate the skin. It is argued that Horrobin generally teaches soft tissue calcification and Kamiya teaches klotho protein-related disorders, both of which fail to shortcomings of Znaden references. It is argued that Kamiya recites "phytic acid" in a list of compounds, and separately recites "ectopic calcification" in a list of disorders that does not combine the two notions to constitute a specific treatment method, and does not otherwise suggest a treatment approach that would cure the shortcomings of the Znaden references.

Applicants' arguments and the evidence provided regarding the penetration of phytate has been considered but not found persuasive because Znaden teaches the same amount of 3% phytic acid that is close to the disclosed amount (2.98%) in the instant application (see example 1). If applicants argue that phytic acid is not dissipated, then instant claims also include phytic acid, in addition to salts of phytic acid. Applicants have not provided any evidence that the amount taught by Znaden does not provide the claimed treatment or prevention whereas the instant claimed "phytic acid" does, notwithstanding the fact that instant claims do not recite any particular amounts of phytic acid or even the formulation that assists in the penetration of claimed phytic acid. Additionally, Prausnitz et al (submitted with instant response) states that the transdermal transport of the negatively charged molecules while challenging can be achieved with the help of chemical enhancers, iontophoresis and ultrasonic methods (last page). Applicants have not provided any evidence how the claimed phytic acid is able to penetrate the layers of stratum corneum that is against the conventional knowledge (inability of phytic acid to penetrate) without any transdermal enhancers, nor

Art Unit: 1611

did they provide any evidence that the additional components of Znaiden do not help in penetration. While instant claims are not limited to phytate, which applicants argue and also disclose as effective for treating ectopic calcification, Znaiden not only teaches phytic acid but also teaches carboxyl derivatives of phytic acid and sulfur derivatives of phytic acid.

Kamiya teaches that the diseases related to klotho-protein expression in humans and animals include ectopic calcification, aging etc., and preferably treated with ornithine and at least one compound selected from phytic acid (0078-0081). Clearly, Kamiya suggests phytic acid to be an active agent in the treatment of any of the above diseases related to klotho-protein expression. Hence, applicant's argument that one would not reasonably expect to extrapolate the teaching of Kamiya et al. to the genus of conditions/diseases associated with a decrease in Klotho protein is not found to be persuasive because ectopic calcification is clearly associated to skin, which is a soft tissue, and one would reasonably expect that topical application of phytic acid would be effective in treating ectopic calcification. Additionally, claim 4 of Kamiya particularly teaches a combination of ornithine and a phosphorus containing compound. Thus, even though Kamiya teaches a number of disorders related to klotho-protein expression, Kamiya suggests phosphorus containing compounds (including phytic acid) in the preferred embodiment. Exemplary rationales that may support a conclusion of obviousness include: Obvious to try " – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success and Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to

Art Unit: 1611

modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. KSR, 550 U.S. at ___, 82 USPQ2d at 1396.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAKSHMI CHANNAVAJJALA whose telephone number is (571)272-0591. The examiner can normally be reached on 9.00 AM -5.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1611

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lakshmi S Channavajjala/
Primary Examiner, Art Unit 1611